Nuclear quantum effects and hydrogen bond fluctuations in water

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The hydrogen bond is central to our understanding of the properties of water. Yet despite intense theoretical and experimental study, it continues to hold some surprises. Here we show, from an analysis of *ab initio* simulations that take proper account of nuclear quantum effects, that the hydrogen bonded protons in liquid water experience significant excursions in the direction of the acceptor oxygen atoms. This generates a small but non-negligible fraction of transient autoprotolysis events that are not seen in simulations with classical nuclei. These events are associated with major rearrangements of the electronic density, as revealed by an analysis of the computed Wannier centres and ^{1}H chemical shifts. We also show that the quantum fluctuations exhibit significant correlations between neighbouring hydrogen bonds, further enhancing the ephemeral shuttling of protons along water wires. We end by suggesting possible implications for our understanding of how perturbations (solvated ions, interfaces, confinement) might affect the hydrogen bond network in water.

Significance Statement: *There is no doubt about the importance of liquid water for climate and life on Earth. But correctly modeling the properties of this substance is still a formidable challenge. Here we show, using state-of-the-art techniques that allow for quantum mechanical effects in the motion of the electrons and the nuclei, that room-temperature water is not simply a molecular liquid: its protons experience wild excursions along the hydrogen bond network driven by quantum fluctuations, which result in an unexpectedly large probability of transient auto-ionization events. Moreover these events are strongly correlated between neighboring bonds, so perturbations that disrupt the hydrogen bond network (pressure, confinement, solvated ions, interfaces) could enhance in a concerted way their impact on water's behavior.*

Introduction

Despite its apparent simplicity, liquid water exhibits a number of anomalous properties, such as a decrease in density on freezing, an isobaric density maximum, and its unusually high dielectric constant and heat capacity [1]. These, together with its unquestionable importance for climate and life on Earth, have made this substance a subject of intense research, both by experiments and simulations.

The central concept that has been used to rationalise the peculiar behaviour of water is that of the hydrogen bond (HB) [2]. The nature of this bond in water has been studied in depth by atomistic computer simulations, which have investigated how it is affected by ionic and electronic polarisability [3, 4], pressure and temperature [5, 6], and nuclear quantum effects (NQEs) [7, 8, 9]. Furthermore, *ab initio* molecular dynamics simulations have been used to shed light on autoionisation [10, 11], a process with profound implications for the chemistry of aqueous solutions.

In this paper we investigate the impact of nuclear quantum effects on the hydrogen bond in pure water, finding a qualitative increase in fluctuations that leads to a partial dissociation of the covalent O–H bond. The weakening of this covalent bond in the presence of hydrogen bonding is consistent with the red-shift of the stretching mode of water upon condensation, and with recent experiments which have demonstrated that selectively exciting the O–H stretch in water leads to a pronounced delocalisation of the proton towards the acceptor oxygen atom [12]. However, the role of nuclear quantum effects in governing the extent of this delocalisation has not been investigated before now.

Our analysis is based on molecular dynamics (MD) simulations of water at different thermodynamic state points, with an *ab initio* description of the interactions between the nuclei. We

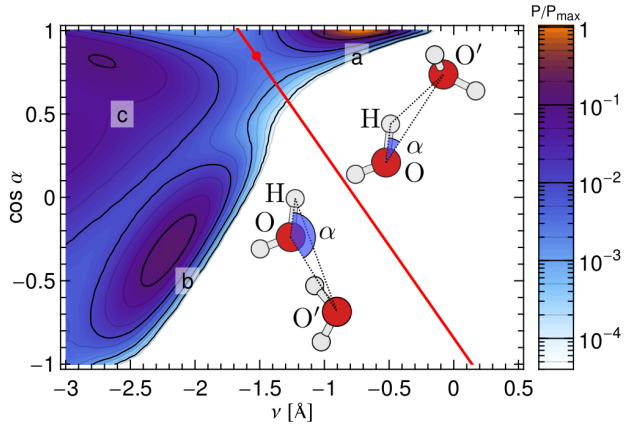

Fig. 1. The joint probability density of finding a O–H–O′ geometry with a given ν-α configuration in a classical simulation of *ab initio* water at 300 K and the experimental density. One can clearly identify: (a) a cluster of hydrogen bonded configurations; (b) a cluster corresponding to the other first neighbours of the tagged molecule. Features at more negative values of ν (c) are less clear-cut. They correspond to farther neighbours, and are irrelevant to the present work. The red line marks the dividing surface one should ideally use to define the hydrogen bonded region, which is obtained by moving away from the saddle point on the probability distribution in the direction of the negative eigenvector of the Hessian.

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also account fully for the quantum nature of the nuclear motion, using a recently-developed combination of imaginary time path integral and coloured-noise thermostatting techniques [13, 14, 15]. The efficiency of this combination allows us to investigate the statistics of the quantum HB fluctuations in *ab initio* water in far more detail than has been possible before. The use of an *ab initio* description of the chemical bonding also allows us to investigate the correlation between HB fluctuations and electronic re-arrangements, and to comment on the implications of our findings for ^{1}H nuclear magnetic resonance (NMR) spectroscopy.

Results

Structural fluctuations of hydrogen bonds in water The analysis we would like to perform requires the definition of one or more structural parameters that (i) clearly identify the protons that are involved in hydrogen bonds, and (ii) characterise HB fluctuations in such a way that makes proton delocalisation apparent. The hydrogen bond in water involves a hydrogen atom H, the oxygen O to which it is covalently bound, and a second, acceptor oxygen atom O′. Different geometric definitions of the HB employ various combinations of the distances between these three atoms. Any such combination contains a degree of arbitrariness, but the essential requirement is simply that the probability density of the chosen structural parameter(s) should be multi-modal [16]. It is this multi-modality that makes it possible to associate HBs with a specific range of parameters in an unambiguous fashion.

The $\widehat{\mathrm{O'OH}}$ angle α is often used as one of the parameters, since it discriminates well between different O′ atoms within the first coordination shell of O. However, it is not very effective in describing fluctuations of the proton, so a second coordinate is needed. Rather than the O–O′ or H–O′ distances, we have chosen to use the proton-transfer coordinate $\nu = d(\mathrm{O–H}) - d(\mathrm{O'–H})$ – a choice that proves to be particularly convenient as we shall see below. Figure 1 shows that the joint probability density relative to ν and $\cos\alpha$ displays a clear-cut clustering in which the hydrogen-bonding region can be defined unambiguously.

In the present study, we shall be more interested in investigating the fluctuations of the proton in well-formed HBs than in resolving borderline configurations. For this purpose, it is clear from Fig. 1 that the proton-transfer coordinate alone suffices to identify configurations in the region $\nu \gtrsim -1.25$ Å as hydrogen bonded, and to characterise the extent of their fluctuations.

Having introduced this analysis framework, let us now use it to investigate the impact of NQEs on hydrogen bond fluctuations. As detailed in the Methods section, the technique we have used to include NQEs combines path integral molecular dynamics – which maps the partition function of a system of distinguishable quantum particles onto the partition function a classical ring polymer consisting of several replicas of the system connected by harmonic springs [17, 18] – with a generalised Langevin equation that reduces the number of replicas needed for convergence (PIGLET [15]).

Figure 2 shows that the impact of NQEs on the HB fluctuations in liquid water is actually quite dramatic – far more so than one would have anticipated on the basis of previous work [7, 8, 9]. We find that quantum protons exhibit broad fluctuations which bring a small but significant fraction of HB configurations (about one in a thousand) into the $\nu > 0$ region – the region that corresponds, at least from a geometric perspective, to autoprotolysis. This should be contrasted with our classical simulations, in which we have only observed negative values of ν and we estimate that the probability of reaching $\nu > 0$ is four orders of magnitude smaller (10^{-7}; see the SI).

One might be tempted to attribute the extreme HB fluctuations seen in our quantum calculations to the excessive charge

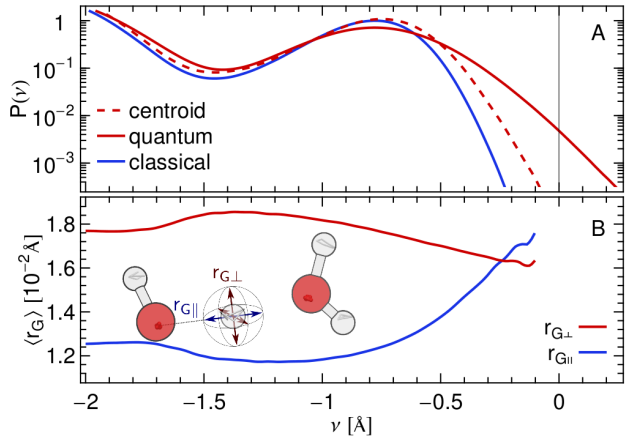

Fig. 2. A. Distribution of the proton transfer coordinate in *ab initio* simulations of water at 300 K. The three curves correspond to a classical simulation, to the distribution of the ring polymer beads in a simulation that includes quantum effects, and to the distribution of the centroid of the ring polymer in the quantum simulation. B. The conditional average of the gyration radius of the ring polymer in the direction parallel ($r_{G\|}$) and perpendicular ($r_{G\perp}$) to the O–H covalent bond for different values of ν for the centroid.

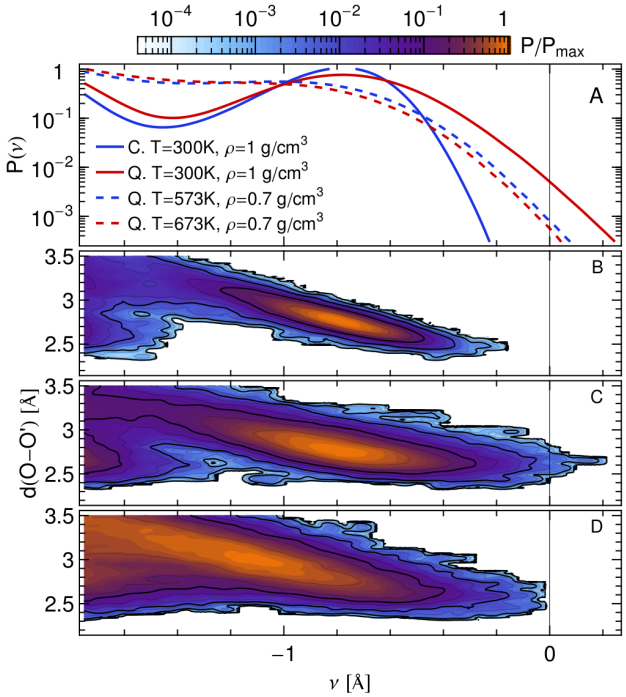

Fig. 3. Panel A shows the distribution of the proton transfer coordinate ν for water at different thermodynamic state points. The lower panels show the joint probability distribution of the proton transfer coordinate and the distance O–O′ between the covalent-bonded and the acceptor oxygen atoms (B: classical nuclei, $T = 300$ K, $\rho = 1.0$ g/cm^3; C: quantum nuclei, $T = 300$ K, $\rho = 1.0$ g/cm^3; B: quantum nuclei, $T = 673$ K, $\rho = 0.7$ g/cm^3).

delocalisation that is known to affect Generalized Gradient Approximation density functionals [19, 20, 21]. However, we have verified that this is a *qualitative* effect that is only slightly altered by the use of a hybrid functional – which typically reduces charge delocalisation [22] – or by other changes to our computational details. As discussed in more detail in the Supplementary Information, the robustness of the effect can be attributed to the large amount of zero point energy in the covalent O–H stretch.

We should stress that the extreme, autoprotolysis fluctuations are very short-lived, and that they are a genuinely quantum-mechanical effect. This becomes clear on examining the distribution of ν for the centre-of-mass of the ring polymer, and its gyration radius in the directions parallel and perpendicular to the covalent O–H bond. The distribution of the centroid along the proton transfer coordinate is only marginally broader than the classical distribution. The transient autoprotolysis events are due to the quantum mechanical fluctuations. Interestingly, the character of these fluctuations changes depending on the position of the centroid along the proton-transfer coordinate. For $\nu \ll 0$, the ring polymer is considerably less spread out in the direction parallel to the stiff covalent bond than in the softer directions perpendicular to it. As the centroid approaches $\nu = 0$, the ring polymer spreads out in the direction parallel to the O–H bond, effectively delocalising onto the acceptor atom O′.

The quantum nature of the extreme HB fluctuations is confirmed by examining their temperature and density dependence. In Fig. 3A we compare the distributions of ν at different thermodynamic state points. Temperature alone has little effect on the fluctuations towards $\nu = 0$: raising the temperature from 573K to 673K actually results in a small *reduction* in the probability of autoprotolysis events, emphasising once more that they cannot be traced to thermal fluctuations. A 30% decrease in the density leads to a more noticeable reduction in the probability of finding the proton at $\nu = 0$. Even this change, however, is still negligible compared to the effect of neglecting NQEs.

Changes in density have the primary effect of modifying the average O–O′ distance. As in the case of solvated proton species [23, 24], one observes a strong correlation between the compression of the O–O′ distance and the excursions along the proton transfer coordinate. A reduction in density leads on average to larger O–O′ distances, and consequently to more negative values of ν. Quantum effects, on the other hand, do not change appreciably the average values of d(O–O′) and ν, but increase significantly their fluctuations around the mean. In light of these observations, it would be interesting to re-visit the problem of autoionisation at high pressure [6], including the effects of quantum fluctuations.

Electronic properties and Wannier analysis We have found that the transient autoprotolysis events are dramatically less common in simulations based on an empirical force field, even when one uses a water model that includes anharmonic terms in the description of the covalent O–H bond [25] (see the

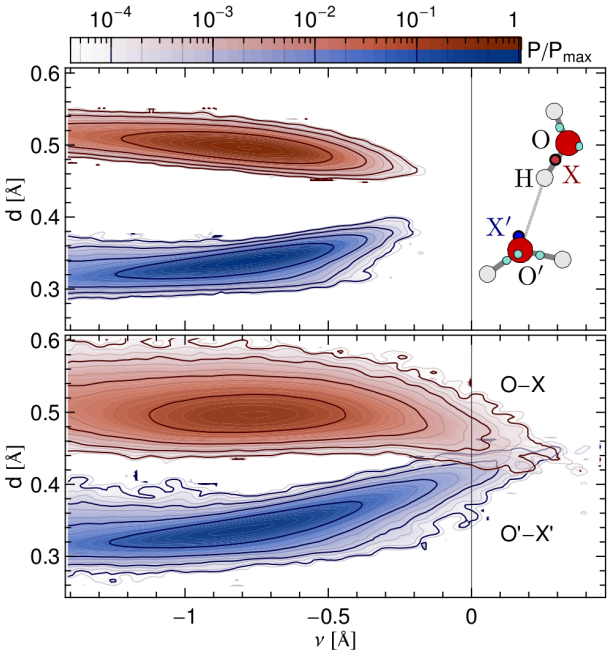

Fig. 4. Given a tagged H atom, the oxygen atom O it is covalently bound to and the acceptor atom O′, X and X′ are the Wannier centres of the two oxygens that are closest to H. The plots report the joint probability distribution of ν and of the distances of the Wannier centres to the corresponding oxygen. The upper panel comes from a classical simulation of liquid water, and the lower panel from a simulation that includes NQEs.

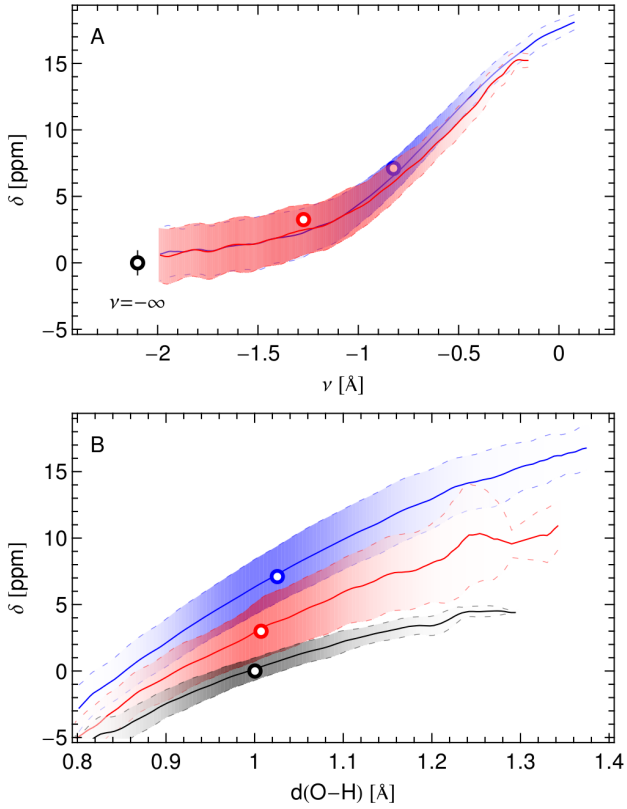

Fig. 5. A compact illustration of the relation between the instantaneous chemical shift and the structural properties of the water hydrogen bond at three different thermodynamic state points: the liquid at $T = 300$ K and $\rho = 1.0$ g/cm^3 (blue), supercritical water at $T = 673$ K and $\rho = 0.7$ g/cm^3 (red), and an isolated gas phase water molecule at 473 K (black). In all cases, NQEs were included using PIGLET. The continuous lines correspond to conditional averages of the chemical shift as a function of the structural parameter, the dashed lines delimit the area within one standard deviation from the mean, and the shading is proportional to the probability distribution of the structural parameter. The dots indicate the means of the structural parameter and the chemical shift. Panel A uses the proton transfer coordinate ν as the structural parameter, the gas phase molecule corresponding to an asymptotic value of $\nu = -\infty$. Panel B uses the covalent bond length $d(\mathrm{O-H})$.

Supplementary Information). This suggests that the extreme fluctuations towards $\nu = 0$ are not due simply to the anharmonicity of the O–H stretching coordinate, but rather that they are stabilised by a re-arrangement of the electron density.

To verify this hypothesis we have analysed our trajectories in terms of their electronic structure. Maximally-localised Wannier functions [26] have been proven in several instances to provide a powerful tool to rationalise the electronic structure of water [4, 8, 6, 5]. The centre of the charge density associated with a Wannier orbital can be thought of as representing an electron pair. Each oxygen atom is surrounded by four such centres. Two are at a distance of ~ 0.32 Å from the atom, and can be interpreted as the lone pairs, while the other two are at ~ 0.5 Å from the oxygen, mid-way between the O and the covalently-bound hydrogens, and can be interpreted as the bonding pairs of the water molecule.

An analysis of the positions of the Wannier centres as a function of ν demonstrates unambiguously that extreme fluctuations of the hydrogen bond are associated with major rearrangements of the electron density (Figure 4). As ν approaches zero for a tagged hydrogen, the electron pair X associated with the covalent bond moves closer to the oxygen atom, approaching the distance characteristic of a lone pair. At the same time, the distance between the lone pair X′ and the acceptor oxygen becomes larger, and approaches the distance corresponding to a covalent O–H bond (Figure 4). This charge transfer is already evident in the classical simulations, but it becomes more pronounced in the simulations with quantum nuclei: in the most extreme cases one even sees an inversion, with $d(\mathrm{O}-\mathrm{X}') > d(\mathrm{O}-\mathrm{X})$.

^{1}H NMR chemical shifts The connection we have made between the structural parameter ν and the electronic structure of the HB can be used to assist the interpretation of experimental results, such as those of ^{1}H NMR spectroscopy. The ^{1}H NMR chemical shift of liquid water from room temperature to above the critical point has been measured using as external reference an isolated water molecule in a dilute gas at 473 K [27, 28]. The observed variations of the chemical shift were linked to variations in the hydrogen bonding as a function of the thermodynamic state point.

Pioneering DFT simulations [29, 30] have obtained qualitative agreement with these experiments. Unfortunately, however, the NMR chemical shift computed by density functional perturbation theory does not yet allow one to achieve the same, exquisite level of accuracy that is characteristic of NMR experiments: details of the calculation such as the exchange-correlation functional, the pseudo-potential and the system size can change the results by more than 1 ppm [31]. On the other hand, simulations do offer useful insight when it comes to unravelling the connections between the chemical shielding of an atom and its environment, since the chemical shielding can be computed for individual atoms in a simulation, while only averages are available to experiments. Furthermore, the ^{1}H NMR chemical shift can be viewed as a concise indicator of the electronic structure in the neighbourhood of a tagged atom, which complements the more complex information that can be extracted from an analysis of Wannier centres.

Early simulations of the isotropic chemical shift δ_{iso} in water and ice found that in the solid state δ_{iso} correlates very well with the elongation of the O–H covalent bond [29]. However, Figure 5 shows that the correlation that is obtained with this structural parameter is highly sensitive to the thermodynamic state point, suggesting that it may not be the most transferable indicator of the connection between structural and electronic fluctuations in water. On the other hand, exactly the same dependence of δ_{iso} on ν is observed at three radically different thermodynamic state points. This clearly indicates that the proton transfer coordinate ν is a more natural structural parameter to use to characterise the electronic re-arrangements associated with hydrogen bonding.

This observation allows us to rationalise some of the qualitative experimental observations of Refs. [28, 27]. The ^{1}H chemical shift of the liquid was observed to decrease with increasing temperature, saturating to a near-constant value in the proximity of the critical temperature. This can be understood by noting that the mean value of the distribution of ν is shifted by density rather than by temperature, and so the chemical shift changes significantly only as long as there is liquid-gas coexistence in the (constant volume) sample holder, and hence the change in temperature produces a change in the density of the liquid phase.

Furthermore, our simulations provide a direct test of the impact of nuclear quantum effects on the chemical shift. As discussed in a recent study of solid-state models of the solvated proton [24], the inclusion of NQEs will not change the experimentally observable (average) NMR chemical shift unless either the instantaneous chemical shift or its fluctuations have a strongly non-linear character. The $\langle \delta_{\mathrm{iso}} \rangle (\nu)$ curve in Fig. 5 is nearly linear from $\nu \approx 0$ to $\nu \approx -1.0$, but it then saturates for $\nu < -1.0$ to a value that corresponds to a broken hydrogen bond, very close to the value for a gas-phase molecule. This kind of non-linear behaviour is precisely what is needed to have NQEs produce a net effect on the average chemical shift.

Our computed average ^{1}H chemical shift relative to a gas-phase molecule at $T = 473$ K amounts at 7.1 ppm for the room-temperature liquid (6.6 ppm for snapshots from a classical simulation, 4.27 ppm in experiments), 3.5 ppm for $T = 573$ K at density $\rho = 0.7\mathrm{g/cm}^3$ (3.1 ppm for a classical simulation, 2.12 ppm in experiments), and 3.0 ppm for supercritical water at $T = 673$ K and $\rho = 0.7\mathrm{g/cm}^3$ (2.8 ppm for a classical simulation). Thus NQEs change the computed δ_{iso} by as much as 0.5 ppm, which is of the same order of magnitude as the errors arising from the use of an approximate description of the electronic structure. Nuclear quantum effects should therefore certainly be included in any future attempt to predict quantitatively the proton chemical shifts in aqueous systems.

Discussion

Provided one singles out major, qualitative effects, *ab initio* computer simulations can contribute a great deal to our understanding of the behaviour of matter at the atomistic level. Here we have shown that quantum mechanical effects in the nuclear motion have a qualitative impact on the HB fluctuations in water – and presumably also in other hydrogen-bonded systems.

Although the competition between intra- and intermolecular quantum effects that appears to be ubiquitous in water reduces the impact of neglecting NQEs on *average* properties [32, 9, 25, 33], the protons should always be treated as quantum particles in studies aimed at capturing rare events, or more generally properties that depend on the tail of the equilibrium distribution. For instance, a recent study [34] suggests that conflicting interpretations of the x-ray absorption spectroscopy of water [35, 36] can be reconciled based on the presence of asymmetric configurations of HBs in water. The enhancement of fluctuations due to the quantum nature of nuclei will inevitably generate a larger fraction of asymmetric configurations (see the SI for a detailed discussion), and may therefore be an important ingredient in the solution of this puzzle.

As we discuss in more detail in the Supplementary Information, the transient autoprotolysis events are strongly correlated across the hydrogen bond network. In our quantum simulations, about one HB in a thousand has a value of $\nu > 0$, so one would expect one chance in a million to find two HBs simultaneously involved in extreme excursions, were they uncorrelated. However, we observe significant deviations from this uncorrelated prediction when we consider pairs of hydrogen bonds around a given water molecule. The probability of the two HBs donated by a water molecule experiencing autoprotolysis at the same time is *reduced* by a factor of ten, and the probability of a simultaneous fluctuation of one donated and one accepted HB involving the same molecule is *increased* by a factor of five, relative to the uncorrelated prediction. This latter scenario corresponds to an ephemeral proton shuttling across a segment of a water wire, similar to what has been seen before in simulations of aqueous protons and hydroxide ions [37, 38, 39].

This, together with the finding that the electronic properties of the hydrogen bond in neutral water correlate very naturally with the proton transfer coordinate, suggests that one could imagine perturbations to the HB network (such as solvated ions, interfaces, confinement, ...) as modulating the stability of the quantum fluctuations[40] that are already present in neat water – rather than introducing completely new effects.

The recent methodological developments we have exploited in this paper [13, 14, 15] have greatly facilitated collecting the extensive data set that underlies our statistical analysis. We anticipate that the routine inclusion of NQEs in *ab initio* simulations, which is made viable by these techniques, will contribute greatly to our future understanding of aqueous systems, including the solvation of the proton and its mobility in bulk water, in confinement [41, 42], and at interfaces.

Materials and Methods

Molecular Dynamics Simulations.. **Ab initio** molecular dynamics simulations were performed using Quickstep, one of the modules of the CP2K package [43]. The electronic structure calculations were based on density functional theory, using the BLYP exchange-correlation functional [44, 45] and GTH pseudopotentials [46]. Wave functions were expanded in the Gaussian DZVP basis set, while the electronic density was represented using an auxiliary plane wave basis, with a kinetic energy cutoff of 300 Ry. We have verified that changing the details of the calculation and the choice of functional does not affect the qualitative conclusions of this work (see the Supplementary Information). We have also performed calculations using q-TIP4P/F, an empirical potential specifically designed to be used in conjunction with path integral simulations [25].

100 ps-long classical molecular dynamics trajectories were performed at constant volume, using a time step of 1 fs, with a stochastic velocity rescaling thermostat [47], starting from a snapshot equilibrated with the empirical force field and discarding the first 6 ps for equilibration. We used the final configurations of these trajectories as the starting point for our simulations with quantum nuclei. These simulations used a path integral molecular dynamics formalism, supplemented with a coloured noise tailored to accelerate convergence [15], so that quantitative accuracy was reached with as few as 6 replicas. The parameters of the coloured noise were downloaded from an on-line repository [48], and are provided in the Supplementary Information. Most of these PIGLET simulations used a time step of 0.5 fs and were 15 ps long, with the first 3 ps discarded for equilibration. The simulation at 300 K was run for a further 35 ps to allow for the slower relaxation time at this temperature than at higher temperatures.

Conditional Averages.. In the text we have presented several conditional averages as a function of the value of the proton-transfer coordinate ν. These quantities correspond to the ensemble averages

$$\langle A \rangle_\nu = \left\langle \delta \left[\nu - \left(\left| \bar{\mathbf{x}}^{\mathrm{H}} - \bar{\mathbf{x}}^{\mathrm{O}'} \right| - \left| \bar{\mathbf{x}}^{\mathrm{H}} - \bar{\mathbf{x}}^{\mathrm{O}} \right| \right) \right] A \right\rangle , \qquad [1]$$

where A is a place holder for any estimator that one might want to average conditionally, $\mathbf{x}_i^{\mathrm{Y}}$ indicates the position of the i-th replica of the atom Y, $\bar{\mathbf{x}}^{\mathrm{Y}} = \sum_i \mathbf{x}_i^{\mathrm{Y}}/P$ indicates the position of the corresponding centroid, and P is the number of path integral beads. For instance, one can define the (directionally-resolved) gyration radius of the ring polymer as

$$\begin{aligned} r_G(\nu)^2 &= \left\langle \frac{1}{P} \sum_{i=0}^{P-1} \left(\mathbf{x}_i^{\mathrm{H}} - \bar{\mathbf{x}}^{\mathrm{H}} \right)^2 \right\rangle_\nu \\ r_{G\parallel}(\nu)^2 &= \left\langle \frac{1}{P} \sum_{i=0}^{P-1} \left[\frac{\bar{\mathbf{x}}^{\mathrm{H}} - \bar{\mathbf{x}}^{\mathrm{O}}}{|\bar{\mathbf{x}}^{\mathrm{H}} - \bar{\mathbf{x}}^{\mathrm{O}}|} \cdot \left(\mathbf{x}_i^{\mathrm{H}} - \bar{\mathbf{x}}^{\mathrm{H}} \right) \right]^2 \right\rangle_\nu \qquad [2] \\ r_{G\perp}(\nu)^2 &= (r_G(\nu)^2 - r_{G\parallel}(\nu)^2)/2. \end{aligned}$$

Wannier Centre Calculations.. All the Wannier centres [26] have been calculated using the algorithm implemented in the CPMD package v. 3.15.1 [49]. The corresponding electronic structure was determined for each frame using fully non-local norm-conserving pseudo-potentials as proposed by Troullier-Martins [50] in combination with a 80 Rydberg plane-wave energy cut-off and a Γ-point sampling of the first Brillouin zone. Our distributions encompass 2000 frames for each trajectory.

Chemical Shift Calculations.. All the ^{1}H nuclear magnetic resonance (NMR) isotropic chemical shieldings (σ_{iso}) have been calculated using the Gauge-Including Projector-Augmented-Wave (GIPAW)[51] method as implemented in the Quantum EXPRESSO package v. 4.3.2 [52]. For each MD simulation discussed in this paper, we calculated the ^{1}H σ_{iso} of 400 frames (2000 frames for the isolated water molecule) uniformly sampled along the trajectory. The electronic structure was calculated using fully non-local norm-conserving pseudo-potentials [50], a plane wave basis with a 90 Rydberg energy cut-off, and a $2 \times 2 \times 2$ Monkhorst-Pack k-point grid [53]. These parameters yield fully-converged ^{1}H σ_{iso} values. The chemical shifts δ_{iso} were calculated using $\delta_{\mathrm{iso}} = \overline{\sigma}_{\mathrm{iso}} - \sigma_{\mathrm{iso}}$, where $\overline{\sigma}_{\mathrm{iso}}$ is the average chemical shielding of an isolated quantum water molecule simulated at 473 K [30].

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